

ORIGINAL ARTICLE

Effect of colostrum given within the 12 hours after birth on feeding outcome, morbidity and mortality in very low birth weight infants: a prospective cohort study

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ABSTRACT

The current study aims to compare the feeding outcome, morbidity and mortality in very low birth weight (VLBW) infants who received early colostrum (<12 hours of life) and those who did not. All VLBW infants admitted to neonatal intensive care unit (NICU) were eligible for the study. Eligible infants were enrolled after obtaining written informed consent from either of the parents. Newborns who received colostrum within the first 12 hours after birth formed the study cohort and all others the control cohort. Both cohorts were followed till discharge from NICU. During the study period, 205 VLBW infants were admitted in NICU of whom 171 (83%) infants were enrolled in the study. Both study groups were comparable for mean birth weight, mean gestation and male sex. The proportion of infants with abnormal Doppler was significantly higher in the control group. All outcomes were adjusted for antenatal Doppler abnormalities. The primary outcome of time to reach full feeds in the study

population was 6.90 ± 4.4 days as compared to 9.80 ± 4.86 days in the control group with a significant weighted mean difference of -2.4 (-0.8 to -3.9) days. Duration of total parenteral nutrition (TPN) days and mortality were all lower in the study cohort. Risk of sepsis and necrotising enterocolitis was similar in the both groups. Enteral colostrum within first 12 hours of birth in VLBW infants reduces the time to reach full feeds, TPN days and mortality.

KEYWORDS

Colostrum; Enteral feeding; Neonates; Preterm; Necrotising enterocolitis; Sepsis.

INTRODUCTION

The enteral feeding for very preterm or very low birth weight (VLBW) infants is often delayed due to concerns of feed intolerance and necrotising enterocolitis (NEC). Colostrum is the first milk produced by the mother, which is unique in its volume, appearance and composition. Colostrum

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is produced when the tight junctions in the mammary epithelium are open which allows the transfer of immunologically derived protective components from the maternal circulation to milk by means of the paracellular pathway [1]. Colostrum is rich in cytokines, growth factors and immunologic components, such as secretory immunoglobulin (Ig)A, lactoferrin and leukocytes. The composition of colostrum of mothers who delivered preterm varies from term with an inverse relationship between concentration of protective factors and duration of pregnancy [2–6]. We could not find any study on early enteral colostrum feeding in VLBW neonates. We hypothesise that the early colostrum feeding can decrease intestinal colonisation with pathogenic bacteria and promote feed tolerance, decrease NEC, sepsis and mortality. The current study compares time to reach full feeds, morbidities (incidence of NEC and Sepsis) and mortality in VLBW infants who received colostrum within 12 hours after birth as compared to those who did not receive colostrum within the 12 hours after birth.

MATERIALS AND METHODS

This prospective cohort study was conducted at Level 3 neonatal intensive care unit (NICU) of the Fernandez Hospital from January 2016 to December 2016. The study was approved by the research and ethics committee of the Fernandez Hospital. Written informed consent was obtained from the parents of eligible infants for study enrolment and publication of medical details. Confidentiality was ensured at all the stages.

All VLBW infants admitted to the NICU were eligible for the study. Patients with perinatal depression (10-minute Apgar score of <5) and major malformations were excluded. All infants had their birth weight recorded in the labour room using an electronic weighing machine. Eligible infants were enrolled after obtaining the written informed consent from either of the parents. Preliminary data, including antenatal and birth details, were documented from the case files. Newborns receiving any enteral colostrum feeds (≥ 1 ml) within the first 12 hours after birth formed the study cohort and all others the control cohort. Every effort was made to encourage the mothers

to express colostrum in the 12 hours after birth. Both cohorts were followed till discharge from NICU or death. During NICU stay, demographic data were recorded, including daily weight monitoring, and weekly, head circumference and length.

Enteral Feeding Policy

Early aggressive nutrition is being followed at our centre. First drip total parenteral nutrition (TPN), Colostrum on day 1 to all if available irrespective of severity of illness. Mothers own milk (MOM) is the preferred choice over donor milk, which is preferred over formula. Feed increments of 10–30 ml/kg depending upon feed tolerance, kangaroo mother care, non-nutritive sucking, oromotor stimulation apply for all VLBW babies. Human milk fortifier is added if the baby is on MOM or donor milk and tolerating 150 ml/kg/day enteral feeds. Tube feeds for <30 weeks and spoon feeds from 30 weeks post-menstrual age.

Data Collection

Feeding details of each enrolled newborn, including duration of enteral feed or parenteral nutrition, time to reach full feeds (defined as enteral feeds of 150 ml/kg/day), were recorded prospectively. NEC was diagnosed in babies, according to the modified Bell staging ≥ 2 [7]. Sepsis was diagnosed if the infant had blood or CSF culture proven sepsis. Death during the NICU stay was considered mortality.

Outcomes

Primary outcome of the study was days to establish full enteral feeding (>150 ml/kg/day) independent of parenteral nutrition. The secondary outcomes of the study included NEC stage ≥ 2 , culture positive sepsis and all-cause mortality prior to hospital discharge.

Sample Size

The average time to reach full feeds in VLBW infants in our unit for the year 2015 was 8 days. With 90% power, confidence level at 95% and assuming that early colostrum would decrease the time to reach full feeds by 1 day from the base line we required 84 infants in each cohort.

Statistical Methods

Descriptive statistics were used to describe baseline variables. Categorical outcome variables were analysed by Chi-square test with continuity correction or Fisher's exact test, wherever one or more expected cell size is less than five. Estimates of the strength of association was deduced by calculating relative risks with their respective 95% confidence intervals. Numerical variables were first tested for normality utilising the Kolmogorov–Smirnov test for normality. Normal distributed independent variables were compared by Student's *t*-test after evaluating equality of variance by Levine's test, whereas a non-parametric test (Mann-Whitney *U*) were used for the variables with a skewed distribution. Linear and logistic regression analysis were done for each outcome adjusting for subjective global assessment (SGA), Doppler abnormality and gestation. All analyses were done using IBM-SPSS v.20 and Microsoft Excel. A *p* value of less than 0.05 was considered significant.

RESULTS

During the study period, 205 VLBW neonates were admitted in our NICU out of whom 171

neonates were included in the study, and nearly equal number of infants got enrolled in both the study cohorts (Figure 1). The mean gestation, mean birth weight and antenatal steroid coverage of the study population were 30.05 ± 2.23 weeks, $1,138 \pm 216.65$ g and 90%, respectively. Both the study groups were comparable in mean weight, mean gestation, SGA status and male sex. The proportion of infants with abnormal Doppler was significantly higher in the control group (Table 1). Linear and logistic regression analysis were done for each outcome adjusting for SGA, Doppler abnormality and gestation.

The primary outcome of time to reach full feeds in the study population was 6.90 ± 4.4 days as compared to 9.80 ± 4.86 days in the control group with significant weighted mean difference of -2.4 days (-0.8 ; -3.9) (Figure 2). The duration of TPN days and mortality was significantly less in infants who have received colostrum in the first 12 hours. The incidence of sepsis and NEC was similar in both the cohorts (Table 2).

DISCUSSION

We have studied the effect of oro-gastric colostrum on nutritional characteristics,

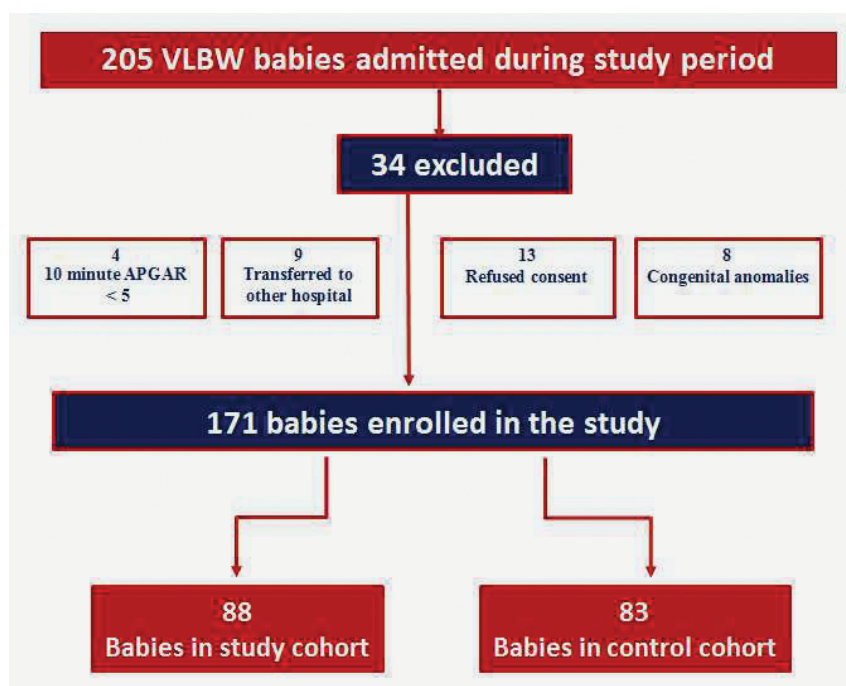


Figure 1. Flow of study.

Table 1. Comparison of baseline variables.

Variable	Control cohort (n = 83)	Study cohort (n = 88)	p-value
Mean weight in grams (SD)	1142.40 ± 214.97	1127.95 ± 225.45	0.668
Mean length in cm (SD)	37.48 ± 2.88	37.72 ± 2.75	0.578
Mean occipitofrontal head circumference in cm (SD)	26.89 ± 1.89	26.83 ± 1.75	0.829
Mean gestation age weeks (SD)	30.18 ± 2.29	29.89 ± 2.18	0.401
Male sex (%)	45 (46)	46 (48)	0.80
SGA (%)	16 (19.7)	21 (23.8)	0.467
Abnormal Doppler (AREDF) (%)	28 (34)	14 (16)	0.007
Antenatal steroids (%)	76 (92)	79 (85)	0.20

AREDF, absent or reversed end diastolic flow in umbilical artery Doppler; SD, standard deviation.

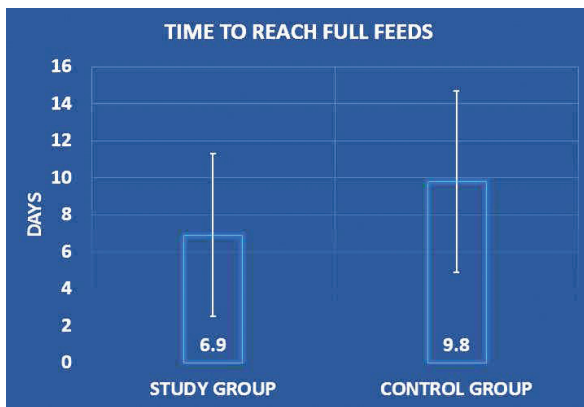


Figure 2. Time to reach full feeds between study group and control group.

morbidity and mortality in VLBW infants. In this study, any amount of enteral colostrum received during the first 12 hours of life improved the nutritional outcomes by decreasing the time to reach full feeds and duration of parenteral nutrition. Study done by Seigel et al. [8] did not show any effect of colostrum in decreasing the time to reach full feeds, but the time for initiation of enteral feeds was earlier in infants receiving colostrum. Route of administration of colostrum was oropharyngeal in the study done by Seigel et al. [8] and in our study, via oro-gastric tube into the stomach. The exact mechanism for decreased duration to reach full feeds is not known, but it may be due to the effect of growth factors on improving the absorptive function, digestion and improved intestinal motility resulting in decreasing the episodes of feed intolerance.

No statistically significant difference was seen in the incidence of NEC among the two cohorts. Similar finding was observed in the study conducted by Seigel et al. [8]. Lack of effect of colostrum on NEC might be because of the low baseline rate of NEC at the study site and the study is not adequately powered to find the difference.

Lower incidence of mortality and a trend towards reduced sepsis were observed in infants receiving colostrum when compared to those who have not. Seigel et al. [8] reported a trend towards decreased mortality in infants who had received early colostrum. There is no definitive mechanism explaining why early colostrum resulted in decreased mortality and sepsis in the study cohort. It is plausible that the various growth factors, immunologically active and antibacterial substances present in the colostrum improve immunity by the process of immunomodulation of cells within the gut-associated lymphoid tissue (GALT) system, and mucosal absorption of factors, including secretory immunoglobulin A (sIgA) and lactoferrin which interferes with bacterial colonisation. Lee et al. [9] reported that oropharyngeal administration of colostrum during the first few days of life increased urinary sIgA and lactoferrin, decreased urinary interleukin-1b, reduced salivary transforming growth factor-b1 and interleukin-8 and reduced occurrence of clinical sepsis in extremely premature infants. A recent Cochrane systematic review including 335 preterm infants

Table 2. Comparison of study outcomes.

Variable	Control cohort (n = 83)	Study cohort (n = 88)	Mean difference or odds ratio (95% CI)*
Time to reach full feeds days (SD)	9.80 ± 4.86	6.90 ± 4.4	-2.4 (-0.8: -3.9)
TPN days (SD)	7.76 ± 5.03	5.56 ± 4.23	-1.7 (-0.3: -3.1)
Sepsis (%)	23 (27.7)	13 (14.7)	0.46 (0.21-1.002)
NEC (%)	7 (8.4)	2 (2.3)	0.26 (0.05-1.3)
Discharge weight in grams (SD)	1,388.79 ± 281.30	1,441.60 ± 236.96	58 (-22: 138)
Mortality (%)	18 (21.6)	3 (3.4)	0.11 (0.03-0.40)
Hospital days (SD)	25.08 ± 16.29	27.5 ± 17.47	3.1 (-2: 8.3)

SD, standard deviation.

*All outcomes are adjusted for antenatal Doppler abnormality.

with gestational ages ranging from 25 to 32 weeks compared the oropharyngeal colostrum with placebo and did not find any significant difference in the incidence of NEC, Late onset sepsis and death before hospital discharge, but infants who received early oropharyngeal colostrum reached full enteral feeds 2.6 days earlier compared to placebo [10]. These results are consistent with our results except for the difference in mortality.

The strength of the study includes the fact that the infants were from a single centre, limiting the treatment centre variability known to occur and affect outcomes. To our best knowledge, this is the first study which has compared early enteral colostrum feeding in VLBW infants. In this study, only gastrointestinal morbidities were evaluated and being an observational study, selection bias can occur even though strict adherence to feeding protocol was exercised during the study period.

In conclusion, enteral colostrum in the first 12 hours in VLBW infants reduces the time to reach full feeds, TPN days and mortality.

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CONFLICT OF INTERESTS

None.

FUNDING

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ETHICS

The study was approved by the research and ethics committee of the Fernandez Hospital. Written informed consent was obtained from the parents of eligible infants for study enrolment and publication of medical details. Confidentiality was ensured at all the stages.

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